Small Rodent Cardiac Phantom for Preclinical Ultrasound Imaging

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Tom Anderson

***Abstract*— Imaging phantoms play a valuable role in quality control and quality assurance of medical imaging systems. However, for use in the relatively new field of small-animal preclinical imaging, only a very few have been described in the literature, and even less or none at all are available commercially. Yet, preclinical small animal phantoms offer the possibility of reducing the need for live animals for test and measurement purposes. Human scale cardiac phantoms, both reported in the literature and available commercially, are typically complex devices. Their designs include numerous flow control valves, pumps and servo motors. These devices are coupled to tissue mimicking materials (TMMs) shaped to replicate the form of cardiac chambers and valves. They are then operated in such a way as to cause the replica TMM heart to move in a life-like manner. This paper describes the design and construction of a small rodent preclinical cardiac phantom which is both of a simple design and construction. Using only readily available materials and components, it can be manufactured without the use of workshop facilities, using only hand-tools. Drawings and pictures of the design are presented along with images of the phantom in operation, using a high frequency preclinical ultrasound scanner.**

Index Terms— cardiac, phantom, polyvinyl alcohol, cryogel, preclinical, small rodent, ultrasound.

I. Introduction

Imaging systems of all types require calibration. This is especially true for medical imaging systems where accuracy and consistency are key requirements. The tests required to achieve these goals are most often accomplished through the use of imaging phantoms. Unlike the use of live subjects for test purposes, phantoms are able to provide consistent and repeatable results, enabling reliable system and process comparisons. The use of phantoms also avoids possible ethical issues related to human or animal use for test purposes [1], [2].

For any one modality phantoms may exist in a range of different formats including:

a) Commercially available precision imaging phantoms, for use as standard test objects in quality control programs (e.g. Leeds Test Objects Ltd, UK.);
b) Commercially available, life-like devices, intended for research or staff training. (e.g. Computerized Imaging Reference Systems, Incorporated, Norfolk, VA. USA.);
c) Virtual phantoms, used in the evaluation of software based imaging schemes. (e.g. www.field-ii.dk);
d) Unique "in-house" devices designed to satisfy a specific need or application [3].

This paper describes the design and construction of a phantom in this last category, designed with a particular application in mind, where no commercially available alternative exists.

Ultrasound imaging is a powerful investigative tool in the rapidly developing field of small animal preclinical imaging. Operating at much higher frequencies than most diagnostic ultrasound systems, developments have essentially followed the same path as medical diagnostic systems, moving from mechanical scan systems to array based scanning. Enabled by this transition, the imaging modes available on diagnostic systems are becoming available on preclinical ultrasound systems. However just as these modes have been, and in some cases continue to be, evaluated in the medical arena, so too they must be evaluated for use in the preclinical imaging field [4]. For the reasons stated above this is often best done using appropriately designed phantoms.

Cardiac imaging is a particular strength of ultrasound given its capability for high frame rate imaging, relatively low cost and rapid through-put. This paper describes the design and construction of a preclinical small rodent cardiac phantom, suitable for evaluation of ultrasonic cardiac tissue imaging modes, such as speckle tracking, strain, elastography and Doppler imaging modes.

II. Requirements

The design of a small rodent cardiac phantom presents its own specific challenges which include:

a) The dynamic nature of the organ to be simulated;
b) Its small size, in the range 10-20 mm diameter;
c) A rapid heart rate, 200-600 beats per minute.

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Existing human scale ultrasound cardiac phantom designs are typically complex devices, involving multiple servo motors, pumps, and controller systems, to induce life-like motion into the phantom materials [5], [6], [7]. However the design goals of the small rodent cardiac phantom described here, were that it should be:

a) Of a simple design, using robust materials to ensure reliability;
b) Formed from tissue mimicking materials;
c) Simulate the movement of the mouse or rat heart;
d) Easy to set-up and use;
e) Constructed from readily available materials;
f) Able to be constructed using only hand-tools.

The simplest, most effective phantoms, are those which are designed to replicate one specific physiological feature or physical phenomenon. The design should also seek to minimize the number of possible confounding factors, such as fluid pulse reflections or multiple reflections of ultrasound pulses. Following from the above argument, the phantom was designed to represent only a single chamber of the small rodent heart, the left ventricle (LV), and to move in a sinusoidal rather than pulsatile fashion. Similarly, it can be argued that from a signal or image processing perspective, that there is little point in attempting to exactly replicate the morphology of the mouse left ventricle. For these reasons the shape chosen was that of an appropriately dimensioned cylinder. This simple shape would minimize manufacturing issues while still allowing a reasonably life-like LV short axis view and wall motion.

III Materials and construction

Typically, dynamic ultrasound phantoms (e.g. cardiac, blood flow) are composed of 4 main elements:

1. A material able to mimic the response of tissue or blood to ultrasound;
2. An actuator mechanism or pump;
3. A controller for flow or rate adjustment;
4. A container or tank.

A. Phantom material

In addition to possessing tissue mimicking characteristics, a material suitable for a cardiac phantom should be elastic in nature to permit expansion and contraction without rupture. Also robustness and chemical stability, conferring "long life" on the phantom, would be valuable. A search of the literature reveals a suitable material to be polyvinyl alcohol (PVA) (Sigma-Aldrich Inc, St Louis, USA.) as a cryogel. In this form it can be readily molded and its physical characteristics modified to provide tissue mimicking characteristics [8], [9].This can be achieved by cycling the material through one or more freeze/thaw cycles.

A number of papers exist detailing how PVA powder can first be made into a gel-like solution (10%)[6], [10], then transformed from a gel into an elastic solid. The freeze/thaw cycling causes chemical cross-linking to occur, transforming the material from a gel to an elastic solid. Further as it is a "bio-compatible" material no particular safety issues are raised by its preparation or use [11], [12].

B. Molding to shape

A PVA cylinder was formed to represent the mouse LV using a simple mold constructed from acrylic tube and rod material, of appropriate sizes. A diagrammatic view of the mold is shown in Fig. 1. The mold barrel consists of a section of acrylic tubing with an internal diameter roughly matching the diameter of the mouse heart at end systole (10 mm). The length of the tube is approximately 45 mm to allow sufficient length for mounting and imaging. The diameter of the "core" of the mold was chosen to roughly match the internal diameter of the mouse left ventricle, also at end systole. The "end seal" of the mold was formed from a short length of acrylic rod, where the external diameter was a tight fit in the mold "barrel". By drilling a recess in this part to accommodate the tip of the core, the core tip would be centered as the mold was assembled. To center the core at the other end, a similar short length of rod was drilled out to a slide fit over the core. A slot was cut in this collar to allow escape of any excess material from the mold, as it was pushed home.

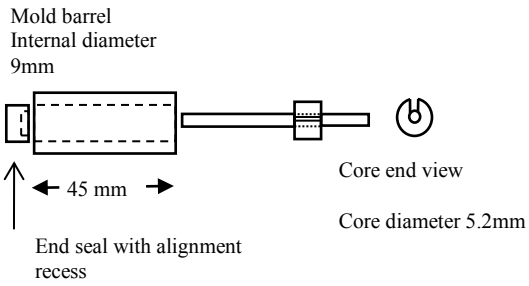


Fig. 1 Diagrammatic view of phantom LV mold components. Using the materials as dimensioned above results in a wall thickness of 1.9 mm.

With the end seal in place, PVA-cryogel solution was injected at the bottom of the mold until full, using a PVA filled syringe and needle. The transparent nature of the acrylic mold and PVA-cryogel, allowed to ensure that the filled mold was free of air bubbles. The core was then inserted till the tip located in the end seal recess and the collar slid down the core, partially into the mold opening. The filled mold was then cycled through a single freeze thaw cycle by means of a -20ºC capable freezer. This was achieved by powering up the freezer from room temperature for 12 hours, then allowing the freezer to return to room temperature, over a further 12 hour period. Following this step, the solid PVA tube was easily removed from the mold, after the end seal and core are pulled free.

Based on the literature [8], this simple protocol was considered to produce PVA with characteristics that were sufficiently tissue-like for the purposes of this exercise.

C. Assembly

The PVA cylinder (henceforth referred to as the "phantom LV") is mounted on a "U" shaped bracket by means of acrylic tubes to which the flexible "flow tubes" are attached. The acrylic tubes themselves, are aligned and held in place by holes in the bracket arms, and secured by threaded screws with wing nuts. This arrangement allows easy placement of the phantom LV on the acrylic tubes. A seal to these tubes, is maintained by means of rubber "O" rings. This assembly is shown in Fig. 2.

The U bracket holding the phantom LV is mounted on the inside of a conveniently sized water tank (length 280 mm, width 70 mm, depth 120 mm) by means of magnets (in this case neodymium extracted from a redundant hard disk drive). One magnet is fixed to the bracket and another, on the outside of the tank, clamps the bracket to the tank wall. Care should be taken when mounting the bracket as magnets of this type are extremely powerful. However, this method of mounting, allows the depth and angle to the horizontal of the phantom LV to be freely adjusted.

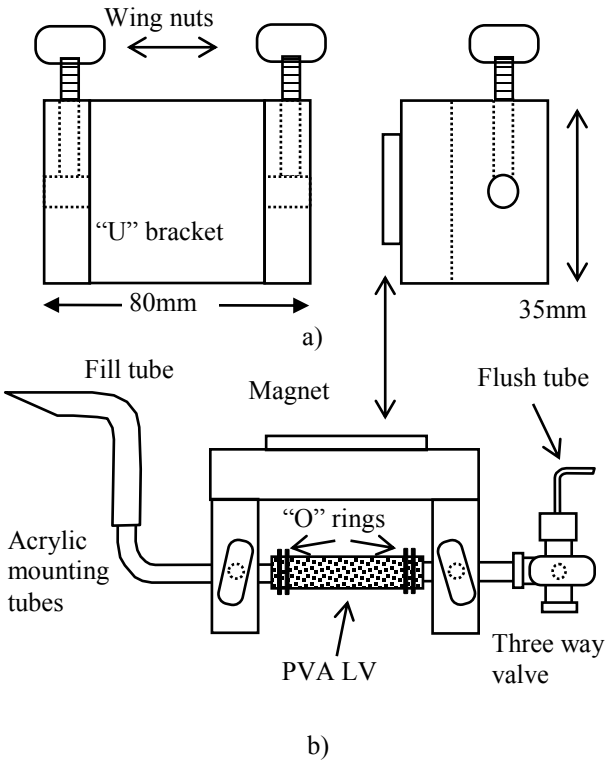


Fig. 2. Diagrammatic views of a) Front and End elevation of the phantom mounting bracket. b) Plan view of bracket and assembled components.

Expansion and contraction of the phantom LV was achieved using a crank driven 1 ml syringe. The crank is formed from a 40 mm diameter wheel, to which the plunger of a 1 ml syringe is attached by means of a swivel bracket. The center point of the swivel bracket is positioned 10 mm from the center of the wheel, resulting in a 20 mm displacement of the syringe plunger (an overall phantom volume increase of 0.2 ml). The outlet end of the syringe is held in a similar swivel attached to a stationary bracket. The crank wheel is mounted on the shaft of a brushless DC motor (BL58EB-35 Watt, Premotec, Dordrecht, The Netherlands). The complete assembly is shown diagrammatically in Fig. 3.

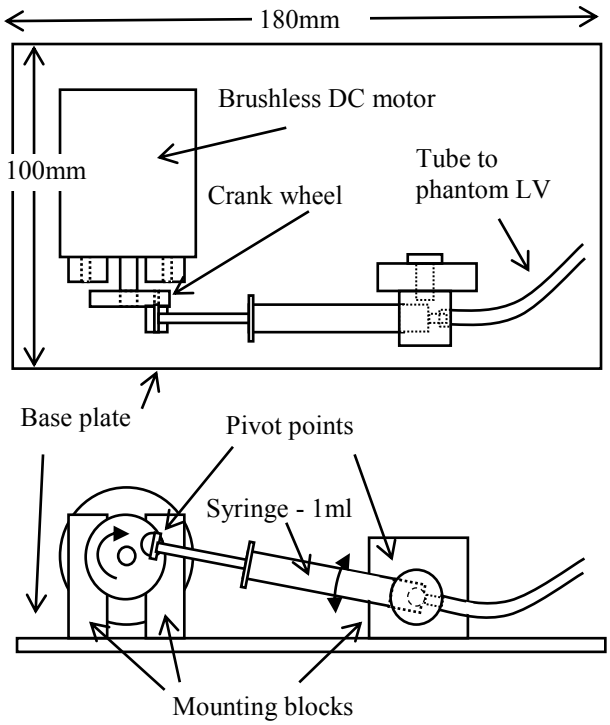


Fig. 3. Line drawing of the phantom motor and pump. Note a three way valve is mounted on the end of the syringe but is not here shown for clarity.

The motor used is of a type where the drive electronics is built into the motor casing and requires only a DC supply voltage (24 V at 2 A), and a signal voltage to control the rate of rotation, and hence "heart rate" of the phantom. This signal voltage was derived from a potentiometer attached across the servo motor supply lines with a series resistor and decoupling capacitor. These resistors form a potential divider limiting the voltage range applied to the motor speed control input, thereby limiting the maximum "heart rate" to that required (650 beats per minute or revolutions per minute). This circuitry is shown in Fig. 4, and was housed in a small box (not shown) along with the connections from the 24 V power supply to the brushless motor. The capacitor serves to minimize any electrical "pickup" or noise on the motor speed control line. The driver electronics also produces a pulse waveform out, the frequency of which is proportional to the speed of rotation. This signal can be used to set an exact "heart rate" if required.

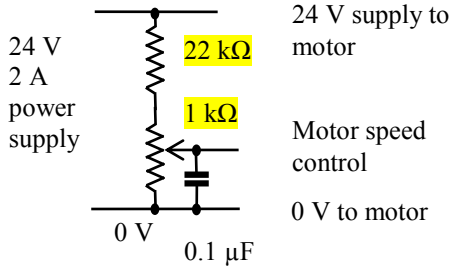


Fig. 4. The speed or rate control components are housed in a small plastic box and wired as shown.

The hydraulic flow diagram is shown in Fig. 5 demonstrating the location of the flow control valves. When in use the valves are first set to allow flushing of the system and removal of all air. Once flushed clear of bubbles, the valves are set to allow flow between the 1 ml syringe and the phantom LV only. In this position, rotation of the motor driving the syringe through the crank, causes expansion and contraction of the LV as water flows to and from the syringe.

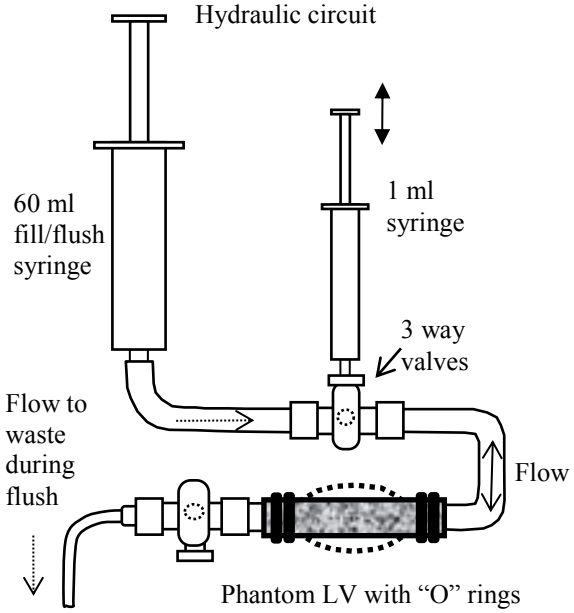


Fig. 5. The hydraulic components of the system.

The principal components used in the construction of the phantom, the drive motor and the PVA are available from a number of suppliers. PVA can be obtained from many chemical and laboratory suppliers both national and international such as Fisher Scientific, Loughborough UK and Sigma-Aldrich, St. Louis, USA.

The drive motor used for this implementation of the device is a 35 watt blushless DC motor with integrated electronics, type BLDC58-35L. As a result of its integral drive electronics the motor requires only a power supply and speed control voltage.

D. Materials List

The majority of materials and components used in the construction of this device are available from multiple sources. The three less widely available items and their suppliers are listed in Table 1

Materials	**Suppliers**
BLDC58-35L 35 Watt brushless DC motor with integrated drive electronics	BL58EB-35 Watt, Premotec, Dordrecht, The Netherlands. Allied Motion Technologies Inc, NY. USA RS Components Ltd, Northants, UK
Polyvinyl alcohol	Fisher Scientific, Loughborough, UK Sigma-Aldrich, St. Louis, USA.
Acoustic absorber	Precision Acoustics Ltd, Watford, UK

Table 1 Principle items used in the construction of the device and their suppliers.

E. Set-up

A picture of the complete system is shown in Fig. 6 with the 60 ml fill/flush syringe and valve in the foreground, and motor/syringe assembly to the left. The water tank and phantom are shown on the right. In the water tank below the phantom LV a section of acoustic absorber (Precision Acoustics Ltd, Dorchester, UK) can be seen. This serves to minimize multiple reflections in the tank and so avoid spurious echoes appearing in the displayed image.

Fig. 6. The fully assembled phantom system with drive motor and water tank.

In common with all other water tank based ultrasound experimental setups it is important to use degassed water to avoid the formation of bubbles, both on the target, and on the transducer face. Degassed water should also be used to fill the phantom, to avoid the build-up of bubbles within the tubing, and in the phantom LV. As described above, filling and flushing the phantom clear of air or bubbles is accomplished by setting the three way valves to allow flow from the 60ml syringe to

waste. Once filled and bubble free, the valves are set so flow can only occur between the 1 ml syringe and the phantom LV.

Using the setup described above, the scanhead of a VisualSonics 770 (Toronto, Ontario, Canada.)was then positioned centrally to obtain a cross-sectional image of the phantom LV. With the speed control variable resistor set to two thirds of its maximum value, power to the motor was applied.

The phantom and water tank are shown in Fig. 7 positioned below the scanhead prior to filling the tank with water.

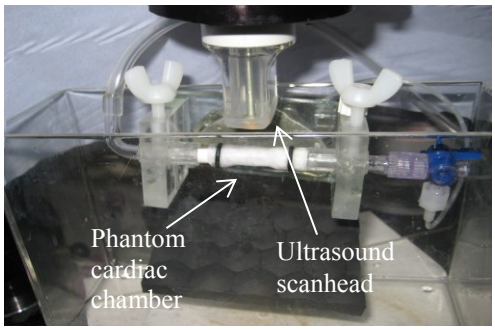
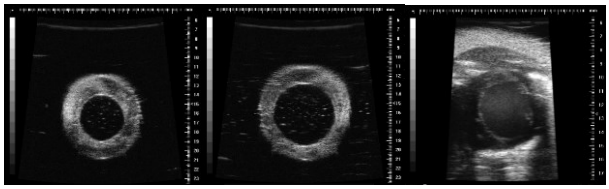


Fig. 7. VisualSonics 770 scanhead (RMV-710 25MHz) positioned above the phantom with acoustic absorber below.

III. Results and Discussion

Captured images of the phantom LV are shown in Fig. 8, representing the short axis view of a mouse or rat heart: a) at "end systole", minimum depression of syringe plunger and b) at "end diastole", maximum depression of the syringe plunger. For comparison image c) shows a short axis view of a mouse LV at end-diastole.



a) b) c)

Fig. 8. Cross section views of the PVA phantom LV at: a) "end-systole", b) "end-diastole", and c) a short axis view of a mouse left ventricle at "end-diastole".

In Fig. 9 a combined B-mode/M-mode image of phantom LV is shown. The M-mode trace demonstrates the expected sinusoidal movement of the phantom walls resulting from the crank drive to the syringe. The "heart rate" measured on the M-mode trace can be seen to be 462 beats per minute, which is within the normal range for an anesthetized mouse [13].

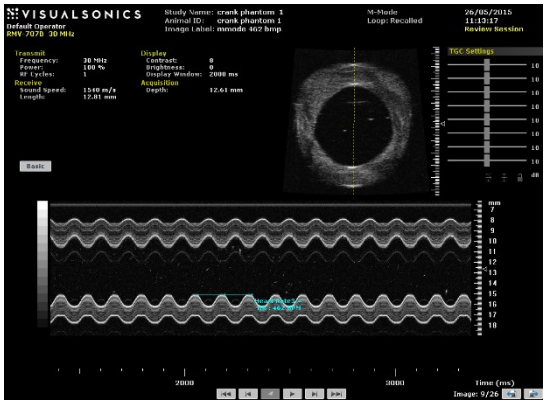


Fig. 9. Duplex view of the phantom LV showing a B-scan image and M-mode trace.

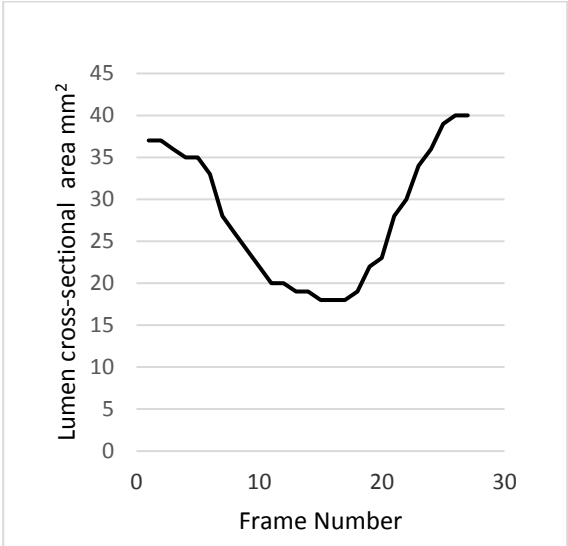


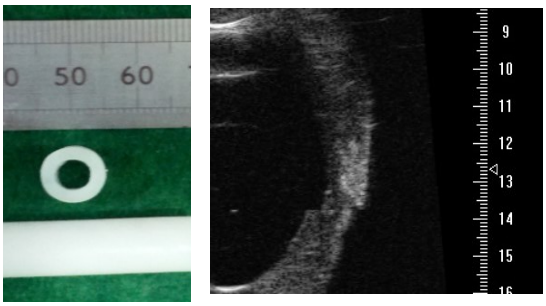
Fig. 10. Graph of changing cross-sectional area of the phantom LV lumen against time (frame number) as measured from a B-mode cine loop with the scanner operating at 462 ultrasound frames/s.

The pre-clinical ultrasound scanner used to demonstrate the phantom, a VisualSonics 770, provides only basic ultrasound imaging modes (B-scan, M-mode and Pulse Doppler). More advanced modes are not available on this machine, not least because of the mechanical nature of the scanhead. However newer model pre-clinician scanners include modes such as Tissue Doppler and speckle tracking which are amenable to evaluation using this device.

In ultrasound, static phantoms play an important role in quality assurance programs and procedures. With their well-defined characteristics, such as target spacing or object sizes, they allow basic machine characterization and performance evaluation. Dynamic phantoms however tend to be much less precise, relying as they do on the movement of liquids or tissue mimicking materials.

In even simple flow phantoms, flow rate varies across the width of the "vessel", while in cardiac phantoms, the extent and velocity of movement is heavily influenced by local geometry, and nearness to fixed boundaries. Though these can be defined as "limitations", they do mirror the situation found in living subjects. The use of dynamic phantoms does have the advantage that precise changes can be made to their operation, such as: doubling the flow rate or the velocity of movement. The ability of the scanning system to correctly interpret these changes can then be assessed.

From careful examination of the phantom images in Fig. 8 it can be seen that there appears to be variations in the wall thickness. Yet, a cross-sectional slice of the actual phantom LV PVA tube (Fig. 11) shows the wall thickness to be constant all round!



a) b)

Fig. 11. a) Picture of the phantom LV PVA tube with a cross-sectional slice from the tube above, demonstrating the constant thickness of the tube wall. b) Image showing a scanner generated discontinuity in the phantom wall.

This apparent inconsistency is the result of variations in the beam width over depth (focusing) and depth attenuation.

Detailed examination of every frame in a cine loop gathered from a dynamic phantom can often reveal problems with image reconstruction which might not be apparent with a static phantom. An example is shown in Fig. 11. b) where a jagged edge mismatch of the phantom wall can be seen. The VisualSonics 770, used to capture this image, is a mechanical scanner so this may be a stroboscopic artifact of some sort.

To date the phantom has been filled with degassed water only. In studies involving boundary detection or Doppler modes for example, the ability to differentiate between blood and tissue can be of interest. This situation could be modeled by filling the phantom with blood mimicking fluid (BMF) thereby forming a BMF/TMM interface. This may seem like an obvious improvement given that it appears to mimic the real-life situation more closely. However as a result of the added complexity great care would need to be taken in interpreting any results obtained.

The phantom, as described, can be readily developed without a dramatic increase in complexity. Improvements could include, the ability to set and change the "heart rate" precisely, as the motor drive electronics provides a pulse waveform out, directly proportional to its rate of rotation. This might also be used to provide an "ECG" signal to assist with area measurement or synchronization with the scanner, for example. The volume change (ejection fraction) could be made adjustable or changeable by fixed amounts, through small changes in the crank arm design, e.g. multiple holes in the crank wheel for the plunger pivot, thereby allowing fixed changes to the "throw" of the plunger, effectively, crank arm length changes. Also the same motor/crank/syringe and feedback arrangement could be used to provide predefined flow rates and profiles for a preclinical scale flow phantom. As an alternative to construction using hand-tools, the base plate and motor/syringe mounts, as well as the U bracket, could readily be formed, using freely available design software, and a 3D printer.

Despite its limitations the phantom provides a useful tool for assessing and comparing the performance of small rodent cardiac systems, as well as providing signals and images that can be used to develop and evaluate signal and image processing methods.

III Conclusion

A preclinical cardiac phantom of the small rodent heart has been described and demonstrated, which is able to replace or reduce the need for live animal subjects for test, training, and scanner evaluation purposes. The device can also function as a source of images and data for computer based signal and image processing developments. The simplicity of design and construction is such that its manufacture can be undertaken in situations where only the simplest of hand-tools are available using readily available materials and components.

Acknowledgment

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